



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/687,262

10/16/2003

Klaus Rudolf

1/1402

9943

28501

7590

06/28/2006

MICHAEL P. MORRIS
BOEHRINGER INGELHEIM CORPORATION
900 RIDGEBURY ROAD
P. O. BOX 368
RIDGEFIELD, CT 06877-0368

EXAMINER

PERLINGER, SARAH E

ART UNIT

PAPER NUMBER

1625

DATE MAILED: 06/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/687,262	Applicant(s) RUDOLF ET AL.	
	Examiner Sarah E. Perlinger	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 May 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) 13 and 14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12, 15 and 16 is/are rejected.
- 7) ☒ Claim(s) 10-12, 15 and 16 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>12/12/03</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-16 are pending. Claims 12-14 were withdrawn from consideration in the Restriction Requirement sent February 21, 2006.

2. ***Election/Restrictions***

Applicant's election without traverse of Group II (claims 1-11, 15-16 as they are drawn to a piperidine compound wherein R2 and R3 form a ring together) in the reply filed on May 31, 2006 is acknowledged. It is recommended that applicants cancel the non-elected subject matter (i.e. claims 1-11, 15-16 drawn to a piperidine compound wherein R2 and R3 do not form a ring together).

In addition, further restriction with regard to claims 10-11 will be required. Claims 10-11, as they are drawn to a physiologically acceptable salt of the compounds according to more than one of claims 1 to 9, or a pharmaceutical composition containing a compound according to more than one of claims 1 to 9, are independent and patentably distinct from groups I-II because compounds and multiple ingredient compositions are not related since patentability of compounds depends on the elements, bonding arrangement, and chemical properties of the compounds, while patentability of a multiple active ingredient composition depends on the ingredients, dosage and ratio of active ingredients and carrier. The classification for the multiple ingredient composition depends on the different active ingredient and without a specific component, classification cannot be ascertained. Therefore, the search for such independent inventions is extremely burdensome and is not coextensive as the search for any of groups I-II.

In the reply filed May 31, 2006 applicants commented that claims 12-14 will be amended to be method of use claims, yet such amendment has not been made. In anticipating such amendment, an evaluation of rejoinder was made.

Claim 12 as it reads on the elected compound, will be rejoined in view of benzodiazepinyl core are known to treat pain.

Claims 13-14 are not rejoinable since no nexus between such a broad scope and the elected compound can be found.

Claims 1-12, 15-16 as they are drawn to compounds and compositions and a process for preparing the compounds and compositions wherein R2 and R3 form a ring together and Y1 is a carbon atom, resulting in a piperidine ring, will be examined on the merits. It is recommended that non-elected inventions be deleted from the claims.

The requirement is still deemed proper and is therefore made FINAL.

3. ***Specification***

The disclosure is objected to because of the following informalities: the application number does not appear on the first page of the specification.

Appropriate correction is required.

4. ***Claim Objections***

Claims 10-12, 15-16 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n). Accordingly, claims 10-11, 15-16 have not been further treated on the merits.

5. Claim 10 is objected to because of the following informalities: it appears the claim contains a typo where, “with inorganic or organic acids or bases inorganic or organic acids or bases” appears. Appropriate correction is required.

6. ***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 12 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in a n improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd. App. 1967) and *Clinical Products, Ltd. V. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

7. ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11, 15-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are indefinite where a “CGRP antagonist of general formula I” is claimed. It is unclear which compounds of the general formula I are CGRP antagonists and therefore the scope of the claims cannot be ascertained.

8. Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as

Art Unit: 1625

the invention. Claim 12 provides for the use of a compound according to at least one of claims 1 to 10, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delineating how this use is actually practiced.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11, 15-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making the compound of general formula I, does not reasonably provide enablement for making the hydrates, mixtures thereof, as well as the hydrates of the salts. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Nature of Invention

The instant claims are drawn to CGRP antagonists of general formula (I), their tautomers, diastereomers, enantiomers, hydrates, mixtures thereof and the salts thereof as well as the hydrates of the salts.

The State of the art and Predictability

Unlike the mechanical art, the high degree of unpredictability is well recognized in the chemical synthetic art. A change in the structure of the compound may drastically affect the rate of the chemical reaction. Furthermore, a high degree of unpredictability in the art exists in utilizing polymorphs as the various polymorphs of a substance can exhibit a variety of different physical properties, which arise from differences in their molecular packing (see Brittain, *Polymorphism in Pharmaceutical Solids*, 1999, pages 5-8).

The amount of guidance and working examples

The Specification (pages 89-102) is limited to teaching one of ordinary skill how to make the compounds of the instant claims. However, these examples do not guide one of ordinary skill in the art in making the hydrates, mixtures thereof as well as the hydrates of the salts of general formula I. In addition, no evidence has been provided that the hydrate, mixtures thereof as well as the hydrates of the salts of general formula I, would have any utility in a pharmaceutical composition or physiologically acceptable salt, or that stable hydrates exist for any of the instant claimed CGRP antagonists. The hydrates, mixtures thereof as well as the hydrates of the salts of general formula I would not necessarily have the same chemical activity as the instant claimed CGRP antagonist and therefore, it is unclear whether or not they could be utilized in a pharmaceutical composition or as physiologically acceptable salts.

Since insufficient teaching and guidance are provided by the specification (pages 89-102), one of ordinary skill in the art, even with a high degree of skill, would not be able to make the hydrates, mixtures thereof, as well as the hydrates of the salts of general formula I without undue experimentation.

10. ***Double Patenting***

Claims 1-11 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of copending Application No. 11/107052 or claims 1-5 of copending Application No. 11/107195 in view of claim 1 of copending Application No. 10/685921. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to the copending claims when A is oxygen, and when R2 and R3 together with the enclosed nitrogen atom form a piperidine or piperazine

ring. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The instant claims are broader than the copending claims where A can be oxygen, sulfur, phenylsulphonylimino or cyanoimino. The difference between the instant claimed compound and the copending compounds is that instead of A only being oxygen, A of the instant claimed compound can be oxygen, sulfur, phenylsulphonylimino or cyanimino. Rudolf et al. however disclosed a structurally similar compound wherein A could be oxygen, sulfur, phenylsulphonylimino or a cyanimino group (see copending Application No. 10/685921, claim 1). One having ordinary skill in the art in possession of claims 1-5 of copending Application No. 11/107052 or claims 1-5 of copending Application No. 11/107195 in view of claim 1 of copending Application No. 10/685921 would be in possession of such modification as A being oxygen, sulfur, phenylsulphonylimino or cyanimino **because** such modification has been clearly guided to one skilled in the art in these references by exemplification of other analogous compounds. All of the references teach piperidine compounds for use in treating migraine or cluster headaches (see 11/107195, claim 6, 11/107052, claim 6 and 10/685921, claim 14). Furthermore, Rudolf et al. demonstrated success in using the structurally similar compounds to treat migraine or cluster headaches (see 10/685921, pages 84-85). One having ordinary skill in

the art would be motivated to make such modification as A being oxygen, sulfur, phenylsulphonylimino or cyanimino knowing that reasonable success has been demonstrated in analogous compounds. It is prima facie obvious to modify one known compound with attributes proven in analogous compounds.

11. Claims 1-11 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of copending Application No. 10/755593 in view of claim 1 of copending Application No. 10/685921. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to the copending claims when A is oxygen, and when R2 and R3 together with the enclosed nitrogen atom form a piperidine or piperazine ring. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The instant claims are broader than the copending claims where A can be oxygen, sulfur, phenylsulphonylimino or cyanoimino and where X can be oxygen, sulfur, an imino group or a methylene group. The differences between the instant claimed compound and the copending compound is that instead of A only being oxygen, A of the instant claimed compound can be oxygen, sulfur, phenylsulphonylimino or cyanimino and instead of X being only a methylene or imino group, X of the instant claimed compound is oxygen, sulfur, imino or methylene. Rudolf

et al. however disclosed a structurally similar compound wherein A could be oxygen, sulfur, phenylsulphonylimino or a cyanimino group and X can be oxygen, sulfur, imino or methylene (see copending Application No. 10/685921, claim 1). One having ordinary skill in the art in possession of claims 1-8 of copending Application No. 10/755593 in view of claim 1 of copending Application No. 10/685921 would be in possession of such modifications as A being oxygen, sulfur, phenylsulphonylimino or cyanimino and X being oxygen, sulfur, imino or methylene **because** such modification has been clearly guided to one skilled in the art in these references by exemplification of other analogous compounds. Both references teach piperidine compounds for use in treating headaches (see 10/755593, claim 10 and 10/685921, claim 14). Furthermore, Rudolf et al. demonstrated success in using the structurally similar compounds to treat headaches (see 10/685921, pages 84-85). One having ordinary skill in the art would be motivated to make such modifications as A being oxygen, sulfur, phenylsulphonylimino or cyanimino and X being oxygen, sulfur, imino or methylene knowing that reasonable success has been demonstrated in analogous compounds. It is prima facie obvious to modify one known compound with attributes proven in analogous compounds.

12. Claims 1-11 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of copending Application No. 11/107189 in view of claim 1 of copending Application No. 10/685921. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to the copending claims when A and X are oxygen, and when R2 and R3 together with the enclosed nitrogen atom form a piperidine or piperazine ring. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The instant claims are broader than the copending claims where A can be oxygen, sulfur, phenylsulphonylimino or cyanoimino and where X can be oxygen, sulfur, an imino group or a methylene group. The differences between the instant claimed compound and the copending compound is that instead of A only being oxygen, A of the instant claimed compound can be oxygen, sulfur, phenylsulphonylimino or cyanimino and instead of X being only oxygen, X of the instant claimed compound is oxygen, sulfur, imino or methylene. Rudolf et al. however disclosed a structurally similar compound wherein A could be oxygen, sulfur, phenylsulphonylimino or a cyanimino group and X can be oxygen, sulfur, imino or methylene (see copending Application No. 10/685921, claim 1). One having ordinary skill in the art in possession of claims 1-5 of copending Application No. 11/107189 in view of claim 1 of copending Application No. 10/685921 would be in possession of such modification as A being oxygen, sulfur, phenylsulphonylimino or cyanimino and X being oxygen, sulfur, imino or methylene **because** such modifications have been clearly guided to one skilled in the art in these references by exemplification of other analogous compounds. Both references teach piperidine compounds for use in treating headaches (see 11/107189, claim 6 and 10/685921, claim 14). Furthermore, Rudolf et al. demonstrated success in using the structurally similar compounds to treat headaches (see 10/685921, pages 84-85). One having ordinary skill in the art would be

Art Unit: 1625

motivated to make such modifications as A being oxygen, sulfur, phenylsulphonylimino or cyanimino and X being oxygen, sulfur, imino or methylene knowing that reasonable success has been demonstrated in analogous compounds. It is prima facie obvious to modify one known compound with attributes proven in analogous compounds.

13. Claims 1-11 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 12-13 of copending Application No. 10/685921 in view of claim 1 of copending Application No. 10/755593. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to the copending claims when R2 and R3 together with the enclosed nitrogen atom form a piperidine or piperazine ring. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The instant claimed compound is broader than the copending compound where V can be chlorine, bromine, amino, methylamino or hydroxyl and where W can be hydrogen, fluorine, chlorine, bromine, iodine, a difluoro or trifluoromethyl group. The difference between the instant claimed compound and the copending compound is that instead of V being an alkyl group, V of the instant claimed compound is a chlorine, bromine, amino, methylamino, or hydroxyl and instead of W being only hydrogen, W of the instant claimed compound is

Art Unit: 1625

hydrogen, fluorine, chlorine, bromine, iodine, a difluoro or trifluoromethyl group. Rudolf et al. however disclosed a structurally similar compound wherein an alkyl group phenyl substituent was an interchangeable phenyl substituent with fluorine, chlorine, bromine, amino, alkylamino or hydroxyl groups and where hydrogen was an interchangeable phenyl substituent with fluorine, chlorine or bromine (see 10/75593, page 130, lines 19-24). One having ordinary skill in the art in possession of claims 1-4, 12-13 of copending Application No. 10/685921 in view of claim 1 of copending Application No. 10/75593 would be in possession of such modifications as V being chlorine, bromine, amino, methylamino or hydroxyl and W being hydrogen, fluorine, chlorine or bromine **because** such modifications have been clearly guided to one skilled in the art in these references by exemplification of other analogous compounds. Both references teach piperidine compounds for use in treating headaches (see 10/75593, claim 10 and 10/685921, claim 14). Furthermore, Rudolf et al. demonstrated success in using the structurally similar compounds to treat headaches (see 10/75593, pages 47-49). One having ordinary skill in the art would be motivated to make such modification as V being chlorine, bromine, amino, methylamino or hydroxyl and W being hydrogen, fluorine, chlorine or bromine knowing that reasonable success has been demonstrated in analogous compounds. It is prima facie obvious to modify one known compound with attributes proven in analogous compounds.

14. **Conclusion**

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Sarah E. Perlinger, whose telephone number is (571) 272-5574. The examiner can normally be reached on Monday through Friday, 8:30 a.m. to 5:30 p.m.

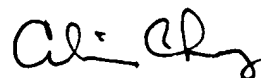
Art Unit: 1625

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Thomas McKenzie, can be reached at (571) 272-0670. The fax number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



06/19/2006



Celia Chang
Primary Examiner
Art Unit 1625